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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,829	02/04/2004	David P. Bingaman	2462 US	3961

7590 01/12/2007

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EXAMINER	
ISSAC, ROY P	
ART UNIT	PAPER NUMBER
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/771,829	BINGAMAN ET AL.	
	Examiner	Art Unit	
	Roy P. Issac	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *30 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application claims priority under 35 U.S.C § 119(e) to the provisional application, U.S. Patent Application Serial No.60/448,943 filed on February 20, 2003.

This Office Action is in response to Applicant's amendment/ remarks/ response filed 30 October 2006, wherein claim 2 has been cancelled, and claim 1 has been amended. New claims 3-18 are submitted. Claims 1 and 3-18 are currently pending, and under examination on the merits.

Rejections Withdrawn

Claim objections to claim 2 under 35 CFR 1.75(c) is withdrawn since claim 2 is cancelled.

Applicant's arguments, see Page 5, paragraphs 3 to page 7, paragraph 2, filed 30 October, 2006, with respect to rejection under 35 U.S.C § 112, second paragraph with respect to the phrases "free of classical preservatives" and "glucocorticoid" have been fully considered and are persuasive. The rejection of claims 1 and 2 under 35 U.S. C 112, paragraph 2, has been withdrawn.

Claim rejections under 35 U.S.C 102(b) over Martidis, Norden and Jonas of claim 1 is withdrawn since claim 1 is amended to add anecortave acetate. The amendement has changed the scope of the claim and the rejections over Martidis, Norden and Jonas are thus withdrawn.

The double patenting rejection based on the co-pending application, 10/545,053 is withdrawn because the conflicting claims are cancelled from the '053 application.

The 102(b) rejection of claims 1 and 2 over Clark et. al. (U.S. Patent No. 6,297,228) is withdrawn because claim 2 is cancelled and the applicant has amended claim 1 to add anecortave acetate.

Cancelled Claims

As indicated above, applicant's arguments/response filed 30 October, 2006 cancelled claim 2. All rejections made with respect to the cancelled claims in the previous office action are withdrawn.

The following are new or modified rejections necessitated by Applicant's amendment filed 30 October 2006, wherein the limitations in all pending claims as amended now have been changed to include the phrase "and anecortave acetate, wherein said composition is free of classical preservatives." Applicants' amendment added claims 3-18. All pending claims depends from claim 1. The limitations in the amended claims have been changed and the breadth and scope of all claims have been changed. Therefore, all rejections from the previous Office Action, filed 30 May, 2006, have been modified or withdrawn and are listed below.

Claim Objections

A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant's sequence will not be changed. See MPEP § 608.01(n). Claim 5 which depends form claim 3 is separated by claim 4. Claims 13-15, which are dependent claims, are separated by claims 7-12 which do not depend from claim 6.

Claims 7-12 and 16-18 are objected to because of the following informalities: Claims 7-12 and 16-18 depends from the cancelled claim 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6 and 13-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 6 is related to compositions comprising triamcinolone acetonide in concentration from **0.4% to 4.0%** w/v. Claim 13 from which claims 14-15 depends, is related to a composition comprising anecortave acetate and triamcinolone acetonide in **0.1 to 6% w/v** and **0.5% to 2.0% w/v** respectively. Applicant's amendment with respect to new claims herein has been fully considered, but is deemed to insert new matter into the claims since the specification as originally filed does not provide support for applicants' claim a composition comprising the **0.1 to 6% w/v** anecortave acetate and **0.5% to 2.0% w/v** triamcinolone acetonide.

Example 5 describes a composition comprising **3%** w/v of anecortave acetate and **0.5 to 4.0%** of triamcinolone acetonide, while the claims herein are directed to ranges of **0.4 to 4.0%** and **0.5 to 2%** of triamcinolone acetonide. The claims herein are directed to ranges of **0.1 to 6%** anceortave acetate while the applicants description for a combination of anecortave acetate in combination with triamcinolone acetonide is only for **3.0%.** Example 1 describes a composition of triamcinolone acetonide in the range of **0.5 to 2.0%.** However, example 1 does not disclose any anecortave acetate in the composition.

The description as originally filed does not provide support for the ranges of triamcinolone acetonide and anecortave acetate as instantly claimed. The specification does not describe any other composition comprising both anecortave acetate and triamcinolone acetonide. The court held that "subgenus

range was not supported by generic disclosure and specific example within the subgenus range"; See e.g. *In re Lukach,* 442 F.2d 967, 169 USPQ 795 (CCPA 1971); the court also held that "a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads" (see *In re Smith*, 458 F.2d 1389,1395, 173 USPQ 679, 683 (CCPA 1972). See also MPEP 2163.

Consequently, there is nothing within the instant specification which would lead the artisan in the field to believe that Applicant was in possession of the invention as it is now claimed. See *Vas-Cath Inc. v. Mahurkar*, 19 USPQ 2d 1111, CAFC 1991, see also *In re Winkhaus*, 188 USPQ 129, CCPA 1975.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 as amended and new claims 3-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3-18 of copending Application No. 10772963 in view of Penn et.al. (PTO-1449, Included by the applicant).

The '963 application is directed to the treatment of pathologic ocular angiogenesis and associated edema by the administration of compositions containing a glucocorticoid and anecortave acetate. The '963 patent does not expressly claim the treatment of nonproliferative diabetic retinopathy or retinal edema.

Cancelled claim 2 of the present application is directed to the use of anecortave acetate in combination with a glucocorticoid for the treatment of nonproliferative diabetic retinopathy and retinal edema.

As discussed above, Penn et. al. teaches that diabetic retinopathy is an angiogenic ocular condition. (Page 283, Column 1, Paragraph 1, lines 3-7). Nonprofilerative diabetic retinopathy is one of the two well known classes of diabetic retinopathies.

It would have been obvious to one of ordinary skill in the art to use glucocorticoids in combination with anecortave acetate for the treatment of nonproliferative diabetic retinopathy and retinal edema.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

Applicants have noted their intent to file terminal disclaimer to obviate the nonstatutory double patenting rejections over applications 10/545,053 and 10/772,963. However, the double patenting rejections will be maintained until terminal disclaimers are received. (MPEP 804(I)(B)).

Applicants further submit that treatments for diabetic retinopathy will not necessarily be effective for treating all pathologic ocular angiogenesis in general. However, the instant application is directed to "retinal edema" as well as "non-proliferative diabetic retinopathy" using a combination of a glucocorticoid and anecortave acetate. The '963 application is directed to the treatment of pathologic ocular angiogenesis and any associated edema using a glucocorticoid and anecortave acetate. The '053 application is directed to the treatment of pathologic ocular angiogenesis and any associated edema comprising the administration of a glucocorticoid and anecortave acetate. As noted in the Office Action dated, 05/30/2006, Penn et. al. teaches that diabetic retinopathy is an angiogenic ocular condition. (Page 283, Column 1, Paragraph 1, lines 3-7). As such, it would have been obvious to one or ordinary skill in the art to use glucocorticoids in combination with anecortave acetate for the treatment of nonproliferative diabetic retinopathy and retinal edema.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejections over Penn in view of Jonas

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Penn et. al. (Form 1449; of record) in view of Jonas et. al (U, PTO-892; of record).

Penn et. al. teaches the use of angiostatic steroids, particularly anecortave acetate in an effective amount for the treatment of angiogenic ocular conditions, including diabetic retinopathy. (Page 283, Column 1, lines 3-11). Penn et. al shows the use of a 10% suspension of anecortave acetate. (Page 284, Column 2, lines 13-18). Nonproliferative diabetic retinopathy is one of the two well known diabetic retinopathies. (Merck Manual of Diagnostics, 12th edition, Page 2384, section "Diabetic Retinopathy," lines 4-7; PTO-892, Of record). Penn et. al. shows that anecortave acetate significantly inhibited pathologic retinal angiogenesis and that it holds therapeutic potential for a number of human ocular conditions in which angiogenesis plays a critical pathologic role. (Page 283, Column 1, Conclusions, lines 5-10). Diabetic retinopathy and specifically, nonproliferative diabetic retinopathy, are angiogenic ocular conditions.

Penn et. al. does not expressly teach that the combination of a glucocorticoid and anecortave acetate is useful in a method to treat diabetic retinopathy or retinal edema.

Jonas teaches the use of cortisone, a glucocorticoid in an effective amount, for the treatment of nonproliferative diabetic retinopathy. (Page 426, Column 1, lines 1-3, and paragraph 2).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a glucocorticoid such as cortisone in combination with anecortave acetate for the treatment of nonproliferative diabetic retinopathy to optimize the effective amounts of active agents in the composition to be administered.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ a glucocorticoid such as cortisone with anecortave acetate for the treatment of nonproliferative diabetic retinopathy.

Therefore one of ordinary skill in the art would have reasonably expected that combining a glucocorticoid with anecortave acetate, both known useful for treating diabetic retinopathy, would improve the therapeutic effects for treating the same disease, and/or would produce additive therapeutic effects in treating the same.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of

combining them flows logically from their having been individually taught in prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Applicant's Examples 1-10 of the specification at pages 6-11 herein have been fully considered but are not deemed persuasive as to the nonobviousness and/or unexpected results of the claimed invention over the prior art. Examples 1-10 provide no clear and convincing evidence of nonobviousness or unexpected results over the cited prior art since there is no comparison to the same present i.e., testing data for the combination method herein in support of nonobviousness for the instant claimed invention over the prior art. Moreover, Example 8, the only example of a combination of anecortave acetate and prednisolone acetate herein merely demonstrate a particular composition.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Response to Arguments

The applicants argue that, the previous office action did not provide motivation for combining anecortave acetate with a glucocorticoid for the treatment of retinal edema or diabetic retinopathy as claimed. Applicants' attention is directed to Page 10, last paragraph of the Office Action dated, 05/30/2006. It has been held *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition to be used for the very same purpose; idea of

combining them flows logically from their having been individually taught in the prior art. See *In Re Kerkhoven*, 205 USPQ, 1069, CCPA 1980. In the instant case, Penn et. al. teaches the use of angiostatic steroids, particularly anecortave acetate for the treatment of angiogeneic ocular conditions including diabetic retinopathy. Jonas teaches the use of cortisone, a glucocorticoid in an effective amount, for the treatment of nonproliferative diabetic retinopathy. As such, the motivation to combine would have flowed from the use of the two compositions for the treatment of diabetic retinopathy.

The applicants further argue that, "even if one would combine the teachings of Penn and Jonas, one would not arrive at the claimed invention, which requires the use of preservative-free formulation of a glucocorticoid and anecortave acetate." The claims of the instant application are directed to "a formulation free of classical preservatives." Neither Jonas nor Penn discuss the use of any classical preservatives in their formulations. As such, one of ordinary skill in the art will not consider the use of any classical preservatives a necessity for the combination of the two compositions.

Rejections over Penn in view Jonas

Claim 1 and 3-6, and 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penn et. al. (Form 1449; Of Record) in view of Jonas et. al (U, PTO-892; Of Record).

The disclosure of Penn et. al. is disclosed above.

Penn et. al. does not expressly disclose the use of a combination of a glucocorticoid and anecortave acetate, or the particular concentration ranges as claimed herein, for the treatment of diabetic retinopathy or retinal edema.

Jonas teaches the use of triamcinolone acrtonide, a glucocorticoid, (20 mg), intravitreally, for the treatment of edema caused by nonproliferative diabetic retinopathy. (Abstract, Page 426, Column 1, paragraph 2; Column 2, Paragraph 2).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a glucocorticoid such as triamcinolone acetonide in combination with anecortave acetate for the treatment of nonproliferative diabetic retinopathy to optimize the effective amounts of active agents in the composition to be administered.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ a glucocorticoid, in particular triamcinolone acetonide with anecortave acetate for the treatment of nonproliferative diabetic retinopathy.

One of ordinary skill in the art would have reasonably expected that combining a glucocorticoid with anecortave acetate, both known useful for treating diabetic retinopathy, would improve the therapeutic effects for treating the same disease, and/or would produce additive therapeutic effects in treating the same.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to

form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980. Furthermore, determining the optimal concentration range for the particular compounds is considered well within the competence level of an ordinary skilled artisan in pharmacological science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

As discussed above, the examples herein do not provide any unobvious or unexpected results.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Rejections over Penn in view Guo

Claim 1 and 3-6, 9-16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penn et. al. (Form 1449; Of Record) in view of Guo et. al (U.S. Patent No. 6,217,895; PTO-892, cited bye the examiner) further in view of Merck Manual (12th Edition, Pages 2384-2386; PTO-892, Of Record).

The disclosure of Penn et. al. is disclosed above.

Penn et. al. does not expressly disclose the use of a combination of a glucocorticoid, in particular prednisolone acetate or fluoromethalone, and

anecortave acetate, or the particular concentration ranges as claimed herein, for the treatment of diabetic retinopathy or retinal edema.

Guo et. al. discloses the use of corticosteroids for the treatment of diseases of retina including ocular inflammation, diabetic macular edema, cystoid macular edema and macular edema. (Column 2, lines 24-52). Guo et. al. further discloses triamcinolone, dexamethasone, flucocinolone, cortisone, predinosolone, flumetholone (also known as flurometholone) and derivatives as examples of useful corticosteroids. Guo discloses a method for delivering a corticosteroid by implanting a sustained release device. (Column 2, lines 24-30).

The Merck Manual of Diagnosis and Therapy teaches that edema is one of the symptoms of nonproliferative retinopathy. (Page 2384, Paragraph 3, titled "Diabetic Retinopathy", lines 5-10). Merck Manual further teaches that macular edema is a common cause of visual impairment in diabetics. (Page 2384, paragraph 3, lines 12-15).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a glucocorticoid such as prednisolone acetate or fluromethalone in combination with anecortave acetate for the treatment of nonproliferative diabetic retinopathy to optimize the effective amounts of active agents in the composition to be administered.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ a glucocorticoid, in particular prednisolone acetonide or flurometholone with anecortave acetate for the treatment of nonproliferative diabetic retinopathy because nonproliferative diabetic retinopathy

has edema associated with it as a symptom and glucocorticoids are well known for their effectiveness against retinal edema and anecortave acetate is well known for its effectiveness against diabetic retinopathy.

One of ordinary skill in the art would have reasonably expected that combining a glucocorticoid with anecortave acetate would improve the therapeutic effects for treating the nonproliferative diabetic retinopathy because anecortave acetate is known for its effectiveness against diabetic retinopathy and glucocorticoids are well known for their effectiveness against retinal edema, a condition associated with diabetic retinopathy.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980. Furthermore, determining the optimal concentration range for the particular compounds is considered well within the competence level of an ordinary skilled artisan in pharmacological science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

As discussed above, the examples herein do not provide any unobvious or unexpected results.

Rejections over Penn in view Drugs & Therapy Perspectives

Claim 1, 3-4 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penn et. al. (Form 1449; Of Record) in view of Drugs & Therapy Perspectives (USPTO-892, Cited by the examiner) further in view of Merck Manual (12th Edition, Pages 2384-2386; Of Record).

The disclosure of Penn et. al. is disclosed above.

Penn et. al. does not expressly disclose the use of a combination of a glucocorticoid, in particular rimexolone, and anecortave acetate, or the particular concentration ranges as claimed herein, for the treatment of diabetic retinopathy or retinal edema.

Drugs & Therapy Perspectives discloses that Rimexolone is effective against ocular inflammation (edema). (Page 1, Paragraph 1). Furthermore, corticosteroids in general and dexamethasone, and prednisolone acetate in particular are also disclosed as effective against ocular inflammation. (Page 1, paragraphs 4-6).

The Merck Manual of Diagnosis and Therapy teaches that edema is one of the symptoms of nonproliferative retinopathy. (Page 2384, Paragraph 3, titled "Diabetic Retinopathy", lines 5-10). Merck Manual further teaches that macular edema is a common cause of visual impairment in diabetics. (Page 2384, paragraph 3, lines 12-15).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a rimexolone in combination with anecortave acetate for the treatment of nonproliferative diabetic retinopathy to

optimize the effective amounts of active agents in the composition to be administered.

One having ordinary skill in the art at the time the invention was made would have been motivated to use reimexolone with anecortave acetate for the treatment of nonproliferative diabetic retinopathy because nonproliferative diabetic retinopathy has edema associated with it as a symptom and rimexolone is well known for their effectiveness against retinal edema and anecortave acetate is well known for its effectiveness against diabetic retinopathy.

One of ordinary skill in the art would have reasonably expected that combining rimexolone with anecortave acetate would improve the therapeutic effects for treating the nonproliferative diabetic retinopathy because anecortave acetate is known for its effectiveness against diabetic retinopathy and glucocorticoids are well known for their effectiveness against retinal edema, a condition associated with diabetic retinopathy.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980. Furthermore, determining the optimal concentration range for the particular compounds is considered well within the competence level of an ordinary skilled artisan in pharmacological science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as

amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

As discussed above, the examples herein do not provide any unobvious or unexpected results.

Rejections over Penn in view Clark et. al.

Claims 1 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penn et. al. (Form 1449; Of Record) in view of Guo et. al (U.S. Patent No. 6,217,895; PTO-892, cited bye the examiner) further in view of Clark et. al. (WO 01/28473; PTO-892, Cited by the examiner).

The disclosure of Penn et. al. is discussed above.

Penn et. al. does not expressly disclose the use of a combination of a glucocorticoid and anecortave acetate or the use of posterior juxtacleral injection as a delivery method.

The disclosure of Guo et. al. is discussed above.

Clark et. al. discloses a method for sub-Tenon delivery of drug depot, in particular anecortave acetate (4,9(11)-Pregnadien-17α,21-diol-3,20-dione-21-acetate), to the posterior segment of the eye. (Page 6, lines 7-15). This delivery is considered a posterior juxtascleral injection. Clark et. al. further discloses the method for the delivery of steroidal anti-inflammatory agents. (Page 13, lines 2-7). Glucocorticoids are considered steroidal anti-inflammatory agents. Clark et. al. further discloses the method for the treatment of cystoid macular edema, which is considered a retinal edema disease. (Page 13, lines 10-13).

Futhermore, Clark discloses that other delivery methods existed in the art have difficulty in administration, and that there exists a need for better delivery methods. (Pages 2-4).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the posterior juxtascleral injection method for the delivery of a combination of glucocorticoid and anecortave acetate for the treatment of nonproliferative diabetic retinopathy because Clark et. al. discloses the use of juxtascleral injection to deliver anecortave acetate and discloses the method as useful for the delivery of other pharmaceutical agents useful for ophthalmic use including steroidal anti-inflammatory agents.

One having ordinary skill in the art at the time the invention was made would have been motivated to use juxtascleral injection method for the treatment of nonproliferative diabetic retinopathy because the posterior jextascleral delivery method disclosed in Clark et. al. allows delivery without some of the limitations existed in the art.

One of ordinary skill in the art would have reasonably expected that the use of posterior juxtasclerical injection of a combination of a glucocorticoid with anecortave acetate would improve the therapeutic effects for treating the nonproliferative diabetic retinopathy because anecortave acetate is known for its effectiveness against diabetic retinopathy and glucocorticoids are well known for their effectiveness against retinal edema, a condition associated with diabetic retinopathy.

As discussed above, the examples herein do not provide any unobvious or unexpected results.

Therefore, the invention as a whole is obvious over the combined teachings of the prior art.

No Claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy P. Issac whose telephone number is 571-272-2674. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

1/8/07

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